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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,728	08/17/2001	Robert Gellibolian	10010543-1	6224

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/932,728	GELLIBOLIAN, ROBERT	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/2003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 17 December 2002 in which claim 16 was amended. The amendments have been thoroughly reviewed and entered. The previous objections to Claim 16 in the Office Action dated 10 September 2002 are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(e) over Goldberg et al and under 35 U.S.C. 103(a) under Goldberg et al in view of Urdea are maintained. The previous rejections over Nilsen are withdrawn in view of Applicant's remarks. All of the arguments have been thoroughly reviewed and are discussed below.

Claims 16-21 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 16 and 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldberg et al (U.S. Patent No. 6,203,989 B1, filed 25 March 1999).

Regarding Claim 16, Goldberg et al disclose a method for covalently binding layers of partially double stranded oligonucleotide linkers onto a polynucleotide-target/polynucleotide-probe pair bound to an array to form a complex that can be detected by analysis comprising: binding an initial partially double stranded oligonucleotide linker to the target/probe pair the initial partially double stranded linker having at least two single-stranded oligonucleotide arms and forming a complex with at least two single-stranded arms; and repeatedly covalently binding one or more next partially double-stranded oligonucleotide linkers to the complex following association of the single-stranded arms of the complex to complementary single-stranded arms of the next partially double-stranded oligonucleotide linker, each one or more next double-stranded linker having a single-stranded oligonucleotide arm complementary to the one or more of the single-stranded arms of the complex and at least one arm not complementary to the single-stranded arms of the next double-stranded linkers (Column 7, lines 4-46; and Claims 1-5).

Regarding Claim 19, Goldberg et al disclose the method wherein each one or more next partially double-stranded oligonucleotide linker has a first end having one single-stranded arm complementary to the one or more single-stranded arms of the complex, a double-stranded body and a second end having two single-stranded arms not complementary to the single-stranded arms of the complex and not complementary to the arms of the one or more next partially double stranded linkers (Column 2, lines 43-67 and Claim 5).

Regarding Claim 20, Goldberg et al disclose the method wherein repeatedly comprises repeatedly covalently binding a first set of partially double-stranded oligonucleotide linkers to the complex and covalently binding a second set of partially double-stranded oligonucleotide linkers to the complex (i.e. successive layers, Column 6, lines 1-14 and Claim 5).

Regarding Claim 21, Goldberg et al disclose the method wherein after covalently binding of the one or more linkers to the complex with n single-stranded arms, the resulting complex has approximately 2n single-stranded arms i.e. at least one non-annealed arm located on the outer surface of the matrix is free (Column 7, lines 26-32).

Response to Arguments

4. Applicant argues that Goldberg et al do not disclose the instantly claimed method. Applicant begins by describing their method. Applicant states that as illustrated in Fig. 10-12 and 15-16, they start with a microarray to which single-stranded probes are bound followed by exposing the microarray to a sample solution containing target molecules. It is noted that a microarray is not claimed. It is noted that a microarray (or array) to which single-stranded probes are bound is not claimed. It is further noted that exposing a microarray (or array) to a sample solution is not claimed. As such, Applicant's comments regarding these elements and method steps are not relevant to the instantly claimed invention or the above rejection.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The instant claims are drawn to method for covalently binding layers of partially double stranded oligonucleotide linkers onto a polynucleotide-target/polynucleotide-probe pair bound to an array comprising: binding an initial partially double stranded oligonucleotide linker to the target/probe pair the initial partially double stranded linker having at least two single-stranded oligonucleotide arms and forming a complex with at least two single-stranded arms; and repeatedly covalently binding one or more partially double-stranded oligonucleotide linkers to the complex following association of the single-stranded arms of the complex to complementary single-stranded arms of the next partially double-stranded oligonucleotide linker, each one or more next double-stranded linker having a single-stranded oligonucleotide arm complementary to the one or more of the single-stranded arms of the complex and at least one arm not

complementary to the single-stranded arms of the next double-stranded linkers. Goldberg et al teach the method as claimed (Column 7, lines 4-46; and Claims 1-5).

Applicant states that probes complementary to subsequences of target molecules form double-stranded target-probe pairs. It is noted that steps of hybridization of forming target probe pair are not instantly claimed. As such, Applicant's comments regarding these elements are not relevant to the instantly claimed invention or the above rejection.

Applicant states that the probe is then extended via primer extension or the target is degraded via exonuclease to create a double-stranded polynucleotide target/probe pair bound to the microarray as instantly claimed. It is noted that microarray and steps of primer extension, target degradation are not recited in the instant claims. As such, Applicant's comments regarding these elements are not relevant to the instantly claimed invention or the above rejection. While the claims do recite a polynucleotide target/probe pair bound, the claims recite limitations for obtaining the target/probe pair. Furthermore, Goldberg et al disclose a polynucleotide target/probe pair as instantly claimed (Column 9, lines 14-34 and Claims 1-23).

Applicant states that an initial partially double-stranded oligonucleotide linker is bound to the target/probe pair which selects only double-stranded target/probe pairs thereby initiating amplification of those microarray features to which target molecules are bound. Goldberg et al discloses contacting an initial partially double-stranded oligonucleotide linker (i.e. matrix monomer) to the target/probe pair as instantly claimed (Column 6, lines 1-65). It is noted that the selection of only double-stranded target/probe pairs, amplification and microarray features are not recited in the instant claims. As such, Applicant's comments regarding these elements are not relevant to the instant claims or the above rejection.

Applicant argues that Goldberg et al do not disclose or suggest binding an initial linker to a probe/target pair as illustrated in Fig. 15. The argument has been considered but is not found persuasive because Goldberg et al disclose binding an initial linker to a probe/target pair

as instantly claimed (Column 6, lines 1-43; Column 7, lines 4-46; and Claims 1-23). While Goldberg et al may not disclose the probe/target pair as illustrated in Fig. 15, they do disclose the method as claimed. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldberg et al (U.S. Patent No. 6,203,989 B1, filed 25 March 1999) in view of Urdea et al (U.S. Patent No. 5,124,246, issued 23 June 1992).

Regarding Claims 17 and 18, Goldberg et al teach the method for covalently binding layers of partially double stranded oligonucleotide linkers onto a polynucleotide-target/polynucleotide-probe pair bound to an array to form a complex that can be detected by analysis comprising: binding an initial partially double stranded oligonucleotide linker to the target/probe pair the initial partially double stranded linker having at least two single-stranded oligonucleotide arms and forming a complex with at least two single-stranded arms; and

repeatedly covalently binding one or more next partially double-stranded oligonucleotide linkers to the complex following association of the single-stranded arms of the complex to complementary single-stranded arms of the next partially double-stranded oligonucleotide linker, each one or more next double-stranded linker having a single-stranded oligonucleotide arm complementary to the one or more of the single-stranded arms of the complex and at least one arm not complementary to the single-stranded arms of the next double-stranded linkers (Column 7, lines 4-46; and Claims 1-5) but Goldberg et al do not teach the initial partially double-stranded linker has a blunt, double-stranded end. However, Urdea et al teach a similar method comprising "covalently binding layers of oligonucleotide linkers onto a target/probe pair bound to an array to form a complex comprising" binding an initial linker to the target/probe pair and repeatedly covalently binding one or more oligonucleotide linkers to the complex (Column 8, line 67-Column 9, lines 30 and Claims 1-11) wherein the initial double stranded linker has a blunt end and wherein the method comprises forming a blunt end on the probe/target pair and ligating the blunt end of the linker to the blunt free end of the probe/target pair (Column 12, lines 30-40 and Fig. 3-2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the sequence-specific hybridization and covalent binding of Goldberg et al with the blunt-end ligation of Urdea et al to thereby provide a sequence independent linker attachment for the obvious benefits of attaching the linkers to any probe/target pair. Specifically, the attachment of the linker to the probe/target pair of Goldberg et al comprises sequence-specific hybridization of the linker to the probe/target pair which results in sequence-specific attachment of the linker. Because the attachment of Goldberg et al is sequence-specific, each sequence requires its own linker. The linker attachment of Urdea et al is via blunt end ligation of the linker to the probe/target pair. This attachment is sequence non-specific. Because the attachment is sequence non-specific, the linker is a universal linker which is attachable to any blunt ended sequence. Therefore, one skilled in the art would have been motivated to modify the sequence-

specific linker attachment of Goldberg et al with the sequence non-specific blunt end ligation of Urdea et al thereby providing a universal linker for the obvious benefits of convenience and economy of linker synthesis.

Response to Arguments

8. Applicant argues that the cited references do not teach or suggest the instantly claimed method of covalently binding an initial partially double-stranded linker to a target/probe pair which initiates target/probe-pair amplification and without which specific target-binding features of the microarray would not be selectively amplified. The argument has been considered but is not found persuasive because as stated above, Goldberg et al disclose binding an initial linker to a probe/target pair as instantly claimed (Column 6, lines 1-43; Column 7, lines 4-46; and Claims 1-23). Furthermore, initiation of target/probe-pair amplification and selective amplification of specific target-binding features of the microarray are not instantly claimed. As such, Applicant's comments regarding these elements are not relevant to the instantly claimed invention or the above rejection.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Usui (U.S. Patent No. 6,261,846 B1, filed 15 April 1999) teaches a method for binding layers of linkers onto a probe target pair.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this

application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
April 28, 2003